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Mulibrey Nanism in a 35 Year-Old Iranian Female with Constrictive Pericarditis

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ABSTRACT

Mulibrey nanism is a rare autosomal recessive disorder characterized by severe growth retardation and pericardial constriction associated with muscle, liver, brain, and eye abnormalities. More than 80% of previously reported cases are Finnish. We report a 35-year-old Iranian female who presented with classic phenotypic features of Mulibrey nanism with symptomatic constrictive pericarditis and underwent pericardiectomy. Our case is one of the rare examples of Mulibrey nanism outside Finland that has been reported so far. (Tanaffos2011; 10(1): 48-51)

Key words: Mulibrey nanism (MUL), Constrictive pericarditis

INTRODUCTION

Mulibrey nanism (MUL) is a rare autosomal recessive disease caused by mutations in the TRIM37 protein of unknown function (1). This protein is located in the peroxisomes suggesting that MUL is a peroxisomal disorder (1). Eighty five of the 110 documented cases with this syndrome are from Finland but sporadic cases have been reported from various ethnic groups all over the world (1). This syndrome is characterized by severe progressive growth retardation from prenatal period until adulthood and multiple organ manifestations in muscle, liver, brain and eye associated with pericardial constriction. An unusual case of Mulibrey

nanism syndrome in a 35 year-old Iranian female is reported in this study. Our case is one of the rare examples of this syndrome occurring outside Finland and the first case reported from Iran.

CASE SUMMARIES

A 35 year-old female was referred to Masih Daneshvari Hospital with shortness of breath and ascites. She was a single woman with progressive dyspnea, peripheral edema and abdominal swelling from 6 months ago that was controlled with high dose diuretics. ECG showed atrial fibrillation (AF) rhythm with relatively rapid ventricular response and digoxin and warfarin were prescribed for her. On physical examination, she was a petite 35 year-old female with significant short stature, low weight (133 cm tall, body weight=21 kg and body surface area=0.9 m²) and unusual dysmorphic craniofacial

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features but without mental retardation. After cardiac evaluation including comprehensive trans-thoracic and tissue-Doppler echocardiography, constrictive pericarditis was suggested and further hemodynamic studies confirmed the diagnosis with no significant pulmonary hypertension (Peak PAP=36 mmHg). Spiral chest CT-scan showed extensive pericardial calcification more frequently in the anterior and inferior aspects of the heart. Moreover, dilated IVC and enlarged liver were noted on the CT scan. Considering her characteristic phenotype (short stature, triangular face, peculiar high pitched voice, thin extremities and hepatomegaly) and pericardial constriction, she fulfilled some of the diagnostic criteria of Mulibrey nanism and we decided to do further work-up for her. Skull x-ray showed a J-shaped sella turcica. X ray of the long bones showed slender long bones. Also, small bell shaped thoracic cage with thin ribs and rounded heart shadow were noted on the chest x ray (Figure 1-3).

Ophthalmologic examination revealed patches of diffuse severe chorioretinal atrophy in both retinae. Her familial history was unremarkable and she was the only member in her family suffering from severe progressive growth failure or nanism. She had primary amenorrhea from puberty and her menstruation was established monthly with hormone-replacement therapy with regular use of Ethinyl estradiol and Medroxyprogesterone. Pelvic ultrasound showed intact uterus and ovaries.

After complete clinical evaluation, she fulfilled most of the diagnostic criteria for Mulibrey nanism syndrome including dysmorphic features (characteristic triangular face with high broad forehead and low nasal bridge, large head relative to stature, thin extremities with proximal relative shortness and narrow shoulder), high pitched voice, severe growth failure, characteristic radiological findings (low, shallow or J-shaped sella turcica), hepatomegaly and retinal abnormalities.

She was scheduled for total pericardiectomy.

After sternotomy and opening up the pericardium, a thick parietal pericardium and especially stony hard visceral pericardium tensely adhered to right ventricle were noted. Total pericardiectomy and decortication of LV were performed for her and samples were sent for pathological analysis. Specimen of pericardium showed fibrohyalinized tissue without granuloma or malignancy. PCR of visceral pericardium was negative for MTB (*Mycobacterium tuberculosis*) complex. Her post-op course was uneventful and she was discharged on the 7th post-op day continuing digoxin and warfarin due to persistent AF rhythm.

Three months after surgery, she was well with normal sinus rhythm (NSR) on ECG. Echocardiographic examination showed resolution of constrictive physiology with normal LV function and we discontinued warfarin and digoxin.



Figure 1. Skull x-ray with J-shaped sella turcica



Figure 2. CXR shows small bell shaped thoracic cage, thin ribs and rounded heart shadow frequently seen in cases with MUL.

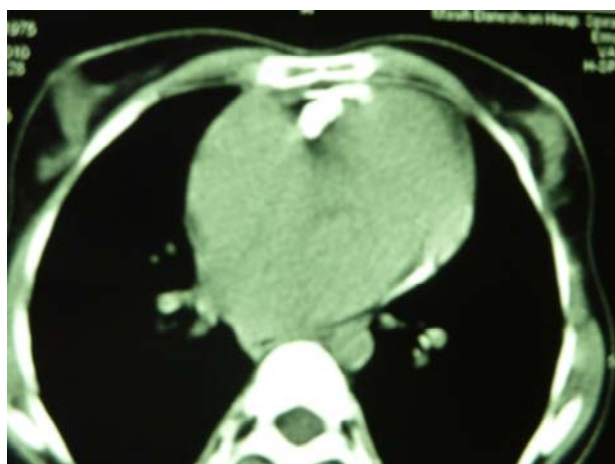


Figure 3. Chest CT scan shows extensive pericardial calcification in anterior and inferior surfaces of the heart

DISCUSSION

To date, we believe that this case is the only example of Mulibrey nanism that has been reported from Iran.

Karlberg and colleagues described diagnostic criteria and clinical features of Mulibrey nanism (1). According to these criteria, Mulibrey nanism was diagnosed in patients with 3 major and one minor or 2 major and 3 minor signs. Our study case showed 4 major signs (1. significant growth failure, 2. craniofacial features, 3. radiological findings on

skull-x-ray, and 4. ocular findings) and 2 minor signs (peculiar high pitched voice and hepatomegaly).

Our case also showed evidence of sexual hormone deficiency that according to Karlberg et al. studies it is seen prevalently in cases with Mulibrey nanism (2,3).

The results of previous reports of this syndrome confirm that Mulibrey nanism is a distinct but variable entity (4,5). The most consistent findings were severe growth failure and characteristic craniofacial features. Organ manifestations varied considerably during life. Constrictive pericarditis (6) with congestive heart failure dominates the clinical state as well as the prognosis (7). However, only 12% of Finnish patients in Karlberg et al review had CHF at the time of diagnosis and half of the adult patients were free of major heart problems (1-3).

In contrast, almost all sporadic cases reported from other parts of the world were notably characterized by a heart disease (8,9).

Presumably while Mulibrey nanism is relatively well known in Finland, elsewhere it is mostly recognized by its characteristic heart disease (10). As the heart involvement is critical for prognosis, its early diagnosis is of most importance (11).

Unfortunately, we could not analyze gene-mutation in this case but considering her phenotype, meeting all the criteria and cardiac involvement (pericardial constriction), there was no doubt about this syndrome in this case.

CONCLUSION

After reviewing all the related literature, we conclude that our patient is the only reported case of Mulibrey nanism from Iran. Mulibrey nanism syndrome should be considered in differential diagnosis of constrictive pericarditis associated with dwarfism and unusual dysmorphic features.

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